

iv formulation of ganciclovir was formulated in saline containing 0.2% HCl at a concentration of 20 mg/mL and administered at a rate of 0.5 mL/kg.

The animals were fasted beginning the evening prior to dosing and until 4 hr after dosing. Blood samples were taken from each monkey at 0 (predose), 5 min (iv only), 15 min, 30 min, 1 hr, 2 hr, 3 hr, 5 hr, 7 hr, 10 hr and 24 hr after dosing. The blood samples were collected in heparinized syringes and the plasma was immediately isolated by centrifugation and frozen at -20° C. until analysis.

#### Assay of Ganciclovir in Plasma

Aliquots of plasma (0.50 mL) were mixed with 0.020 mL of internal standard (acyclovir, 15 µg/mL in 10% methanol/water) and 3.0 mL of acetonitrile. The mixture was vortexed and the resulting precipitate was removed by centrifugation (4,000 g, 10 min). The supernatant was evaporated to dryness under nitrogen and reconstituted in 200 µL of HPLC mobile phase. Aliquots (0.05 mL) were analyzed by HPLC using a Keystone Hypersil BDS, 250x4.6 mm C 18 column. The mobile phase contained 2% acetonitrile in 30 mM sodium phosphate buffer containing 5 mM heptane sulfonic acid, pH 2.0 and was pumped at 1.0 mL/min. Ganciclovir and internal standard were detected and measured by UV absorbance at 254 nm.

The bioavailability (F) is calculated according to the equation given in Example 9.

The prodrug 2-(2-amino-1,6-dihydro-6-oxo-purin-9-yl)methoxy-3-hydroxy-1-propanyl-L-valinate had an oral bioavailability of 35.7%. 2-(2-Amino-6-dihydro-6-oxo-purin-9-yl)methoxy-1,3-propanediyl bis (L-valinate) had an oral bioavailability of 23.5%. Ganciclovir has a bioavailability of 9.9%. Giving the same prodrug orally and ganciclovir iv to the same monkeys results in a mean oral bioavailability for the prodrug of 41.6%.

#### EXAMPLE 11

The following examples of the proposed ganciclovir L-valine monoester capsules contain as excipients povidone, a binder; corn starch, a disintegrant; and stearic acid, a lubricant and glidant; which are filled into a two piece hard gelatin capsule shell. Water is the granulating liquid, and is essentially removed during processing.

Quantitative Composition of Ganciclovir L-Valine Monoester Capsules  
(One Capsule Three Times Per Day)

Ingredients	Weight Per Capsule (mg)	% W/W
Ganciclovir L-valine monoester hydrochloride	390.00	92.75
Povidone	12.61	3.00
Corn starch	16.81	4.00
Stearic acid <sup>1</sup>	1.05	0.25
Water <sup>2</sup>		
Total fill weight (theoretical) <sup>3</sup>	420.47	100.00

The powder blend is filled into two piece hard gelatin capsule shells.

<sup>1</sup>The amount of stearic acid may vary from 0.1% to 5.0% of the weight.

<sup>2</sup>The amount of water may vary to produce an acceptable granulation, and is dried off.

<sup>3</sup>The total fill weight (theoretical) does not include the residual moisture that will be present in the finished product.

Quantitative Composition of Ganciclovir L-Valine Monoester Capsules  
(Two Capsules Three Times Per Day)

Ingredients	Weight Per Capsule (mg)	% W/W
Ganciclovir L-valine monoester hydrochloride	312.00	92.75
Povidone	10.09	3.00
Corn Starch	13.45	4.00
Stearic Acid	0.84	0.25
Water <sup>2</sup>		
Total fill weight (theoretical) <sup>3</sup>	336.38	100.00

<sup>1</sup>The amount of stearic acid may vary from 0.1% to 5.0% of the weight.

<sup>2</sup>The amount of water may vary to produce an acceptable granulation, and is dried off.

<sup>3</sup>The total fill weight (theoretical) does not include the residual moisture that will be present in the finished product.

The powder blend is filled into two piece hard gelatin capsule shells.

#### Example of the Manufacturing Procedure for Ganciclovir L-Valine Monoester Capsules

1. Blend the ganciclovir L-valine monoester and part of the corn starch in a suitable manner.
2. Dissolve the povidone in the water with stirring.
3. Add (2) to (1) while continuing to mix to form a granulation.
4. Mill the wet granulation if necessary.
5. Dry the wet granulation in a dryer.
6. Pass the dry granulation, the remaining corn starch, and the stearic acid through a mill.
7. Blend (6) in a suitable mixer.
8. Encapsulate the appropriate amount of (7) into 2 piece hard gelatin capsule shells.

What is claimed is:

1. The compound 2-(2-amino-1,6-dihydro-6-oxo-purin-9-yl)methoxy-3-hydroxy-1-propanyl-L-valinate hydrochloride in crystalline form.

2. An antiviral pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable excipient.

3. A method of treating an animal infected with a virus selected from herpes simplex virus and cytomegalovirus, comprising administering a therapeutically effective amount of the compound of claim 1 to the animal.

4. The method of claim 2 where the compound is administered orally.

5. The method of claim 3 where the herpes viral infection is a cytomegalovirus infection.

6. The method of claim 5 wherein the compound is administered orally.

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